UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF

PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 15 MAY 2007

SUBJECT: FIPRONIL - Occupational Exposure/Risk Assessment for the Proposed Use of AMULET™ C - L Fruit Fly Stations

PC Code: 129121 DP Code: 339791, 332648

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INTRODUCTION

Under provisions in Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, BASF Corporation has requested registration of the insecticide fipronil for use in Fruit Fly Baits or Traps.

This memorandum serves as the RD's assessment of exposure and risk to occupational pesticide handlers (mixers, loaders, applicators) and to agricultural workers. It should be noted that the risk assessment techniques used in this document are those that have been developed and refined by the Health Effects Division (HED)/Office of Pesticide Programs' Science Policy Council for Exposure (ExpoSAC). Therefore, the risk assessment methods are the same as those used by HED and are HED standard operating procedure (SOP).

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USE PATTERN SUMMARY

The use pattern summary is abstracted from the proposed product label. The product proposed for use is Amulet™ *C-L Fruit* Fly Stations. The product is formulated into strips of about 1.0 inches x 2.0 inches of material resembling cellulose egg carton material (i.e., not plastic foam). Each strip is considered 1 bait station and each contains 0.00071 oz active ingredient (*ai*) *fipronil* (*0.000044* lb ai). The product also contains 4-(p-Hydroxyphenyl)-2-butanone, acetate (Cue-Lure) which is an attractant to certain male Dacine fruit flies. Male flies are attracted to the bait or trap, make contact and subsequently die. The object is to reduce fly populations by reducing the possibility of successful matings and egg production.

For product placement the label states: "Wear gloves when handling Amulet C-L stations. Remove Amulet C-L stations from the sealed packet and, using twist ties provided, hang each station from a twig within shady foliage of shrubs or trees out of reach of children. Hang in full shade, as exposure to direct sun, wind and heavy rainfall may reduce the effective life of Amulet C-L stations."

"For use in fruit fly traps, place one Amulet C-L station per trap. Hang trap in complete shade. Traps may be placed in non-crop vegetation, or in orchard below fruit." It should be noted that the traps resemble clear plastic drinking cups with one end closed and the end with an access hole of about 1.0 inch diameter. A bait station is placed inside the trap and the trap hung as described on the label.

The label indicates the bait stations may be distributed aerially by helicopter or small fixed wing aircraft flying at 25-31 mph. The ties are attached to the station such that there is a 1.0 in hook fashioned at the end and the single units are dropped from the aircraft at 2 - 4 second intervals while flying transects over a selected area. Such applications are limited to inaccessible forest and away from waterways.

The rate of application is 10 - 20 bait stations (or traps) per acre. The product label directs personal protective equipment be worn consisting of long-sleeved shirt, long pants, chemical resistant gloves and shoes plus socks.

The label indicates that bait **stations** may need to be replaced every 3 months (90 days) and that the strips used in **traps** may need to be replaced every 4 months (120 days).

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

HED and RD typically utilize standard operating procedures (SOP) to assess exposures and risks to occupational pesticide handlers. The proposed use pattern is somewhat unique and there are no SOPs, in the strict sense, with which to assess exposure. In this case ARIA/RD utilizes the basic concepts of the standard procedures however modifications are made where certain data are not available.

For the proposed use pattern, there is no typical mixer/loader activity as is associated with the majority of agriculturally related pesticide applications. There are "applicators", i.e., individuals who hang the bait stations or traps or who eject the stations or traps from aircraft.

HED and RD rely upon data in the Pesticide Handlers Exposure database (PHED) to describe occupational exposures. The PHED data comprise a collection of data that reflect occupational pesticide handler exposure. The data were collected during exposures studies of persons performing various methods of mixing and loading in preparation for application. Other studies measured exposures as a result of many methods of application. The data are termed "unit exposures" and are expressed as mg of active ingredient per pound of ai handled during the work activity. There are no unit exposure data for this method of application (hanging bait stations or traps). The PHED contains unit exposure data for several methods of mixing and loading and the unit exposures are summarized below.

Mixing/Loading Using a single layer of work clothing AND protective gloves

	Dermal (mg ai/lb ai handled)	**Inhalation (mg ai/lb ai handled)**
Dry flowable open load.....	0.066	0.00077
Granular open load.....	0.0069	0.0017
Liquids open load.....	0.023	0.0012
Wettable powder open load	0.17	0.043
Wettable powder in water soluble packages.....0.0098		0.00024

The PHED does contain unit exposure data for an applicator hand dispensing granular bait while wearing protective gloves.

71.0	0.47

ARIA/RD notes that none of the unit exposures presented above are considered a good "fit" for the proposed use pattern. Most of the applicator unit exposures in the PHED describe exposure due to some form of spray application, dust application or mechanized granular application and are not suitable for use regarding the proposed use pattern.

Although not a good "fit", ARIA/RD proposes use of the unit exposure for an applicator hand scattering granular bait. Since it is the highest unit exposure, it is thought to provide a conservative, screening level assessment.

Another major uncertainty is the number of acres that may be treated per day by an individual. This is a rather unique method of application and ARIA/RD does not have data which describe the numbers of acres that might be treated. HED and RD assume 40 acres of tree fruit or tree nuts may be treated per day with a high-volume air-blast sprayer. It is assumed that 40 acres of golf course may be treated per day using ground-boom sprayers. There are no "standard" scenarios that might apply to the proposed use pattern. Again, for purposes of a screening level, conservative assessment, it is assumed 40 acres per day may be treated. That is likely an overestimate.

The SOP methodology is:
Unit exposure * application rate * units treated/day ÷ body weight. In this case there is no adjustment for dermal absorption since the dermal toxicological endpoints are derived from a dermal study.

The Agency's most recent consideration of the fipronil toxicological database was presented in November 2005 (B. Hanson, DP Codes, 316795, 322527, 322529, Memo 15 NOV 2005, "Petition Number: 05OR18 - Human Health Risk Assessment for Fipronil - Incorporating the Section 18 Proposal for the Use of Fipronil on Turnips and Rutabagas in Oregon and the Renewal Request for use of Fipronil on Corn."). In the Agency's review a short-term duration (1 - 30 days) dermal toxicological endpoint was identified from a 21-day dermal toxicity study in the rabbit. The No Observable Adverse Effects Level (NOAEL) is 5.0 mg ai/kg bw/day and the toxic effects noted were decreased body weight gain and food consumption in both sexes. A 70 kg body weight is used to calculate exposure.

A short-term duration inhalation endpoint was identified from a developmental neurotoxicity study in the rat. The NOAEL is 0.05 mg ai/kg bw/day and the toxic effects seen were decreased in group mean pup weights during lactation and significant increase in time of preputial separation in males. Since the inhalation toxic effects were identified from a developmental study with fetal effects, a 60 kg bw is used to calculate inhalation exposure. See Table 1.0 for a summary of estimated exposures and risks and see the ATTACHMENT for a summary of toxicological endpoints used for risk assessment.

Table 1.0 Summary of Exposure & Risk for Occupational Handlers Applying Fipronil in Fruit Fly Baits and Traps

Unit Exposure[1] mg ai/lb handled	**Applic. Rate**[2] lb ai/unit	**Units Treated**[3]	**Avg. Daily Exposure**[4] mg ai/kg bw/day	**MOE**[5]	**Combined MOE**[6]
Dermal: SLWithGlove 71.0 Inhal. 0.47	0.000044 lb ai/station and 20 stations/A	40 A/day	Dermal: SLWithGlove 0.036 Inhal. 0.00028	140 179	80
Dermal: SLWithGlove 71.0 Inhal. 0.47	0.000044 lb ai/station and 20 stations/A	5 A/day	Dermal: SLWithGlove 0.00446 Inhal. 0.0000345	1121 1449	630

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled.
2. Applic. Rate. = Taken from the proposed label
3. Units Treated are assumed by inference from other SOP
4. Average Daily Dose (ADD) = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (60 kg for inhalation since NOAELs are identified from a developmental study with fetal effects and 70 kg for dermal).
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. NOAEL = No Observable Adverse Effect Level (5.0 mg a.i./kg bw/day for short-term dermal and 0.05 mg ai/kg bw/day for inhalation)
6 Combined MOE = $\frac{1}{\frac{1}{MOE_{Dermal}} + \frac{1}{MOE_{Inhalation}}}$

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to fipronil used as proposed. If 40 A/day are treated, the combined MOE is 80. Under other circumstances, that would likely be of concern to ARIA/RD. However, due to the highly conservative nature of the assumptions used in the assessment, the MOE of 80 does not exceed ARIA/RDs level of concern.

The unit exposure figure for spreading granular baits by hand is believed to be a higher measure of unit exposure than would be measured for workers hanging fipronil baits or traps. The unit exposure for open loading of wettable powder is 0.17 mg ai/lb ai handled nearly 400 times less. Neither method is reflective of dispersing the fruit fly baits or traps. Further, the assumption of 40 acres treated per day is likely an overestimate of application ability. Finally, if the baits or traps remain effective for 90 - 120 days (depending on which method is used), then the bioavailability of fipronil, on a daily basis, is expected to be very small.

ARIA/RD also estimated exposure and risk based on 5 acres treated/day. The combined MOE is 630. In 2002, ARIA notes that the median farm size in Hawaii was 6 acres. While there is uncertainty with regards to the size of treatment blocks, ARIA/RD believes the proposed use pattern does not exceed its levels of concern.

POST-APPLICATION EXPOSURE

ARIA/RD believes post-application exposure would be negligible. The product is efficacious for 90 - 120 days depending upon method of application. Once the product in placed in a tree canopy, there is no need for further contact. Traps may be visually monitored since the bait is enclosed in a clear plastic device therefore no contact is expected. Assessment of post-application exposure is considered unnecessary, based upon the proposed use pattern.

RESTRICTED ENTRY INTERVAL (REI)

No REI is stated on the proposed label.

ATTACHMENT

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations including infants and children	NOAEL= 2.5 mg/kg UF = 100 **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = acute RfD / FQPA SF = 0.025 mg/kg	Acute neurotoxicity - rat LOAEL = 7.0 mg/kg based on: decreased hindleg splay in males at 7 hours.
Chronic Dietary all populations	NOAEL= 0.019 mg/kg/day UF = 100 **Chronic RfD** = 0.0002 mg/kg/day	FQPA SF = 1 **cPAD** = chr RfD / FQPA SF = 0.0002 mg/kg/d	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Oral (1-7 days) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Intermediate-Term Oral (1 week - several months) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Short-Term Dermal (1-7 days) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Intermediate-Term Dermal (1 week - several months)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.

(Occupational/ Residential)		(Residential, includes FQPA SF)	
Long-Term Dermal (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Inhalation (1-7 days) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat *LOAEL = 0.90 mg/kg/day based on:* decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Intermediate-Term Inhalation (1 week - several months) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) ***LOC for MOE** = 100* (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during *lactation, and significant increase in time of* preputial separation in males (dietary).
Long-Term Inhalation (several months - lifetime) (Occupational/ *Residential)*	oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = *100%)*	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, *includes* FQPA SF)	Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Cancer (oral, dermal, inhalation)	Group C - possible human carcinogen	Use chronic RfD to estimate human risk	Increases in thyroid follicular cell tumors with fipronil (male/female)

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

NOTE: The ATTACHMENT is taken from: (B. Hanson, DP Codes, 316795, 322527, 322529, Memo 15 NOV 2005, "Petition Number: 05OR18 - **Human Health Risk Assessment for Fipronil** - Incorporating the Section 18 Proposal for the Use of Fipronil on Turnips and Rutabagas in Oregon and the Renewal Request for use of Fipronil on Corn.").

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13544

R144667

Chemical: Phosphamidon

PC Code:
018201
HED File Code: 13100 Other Tox Documents
Memo Date: 7/25/1988
File ID: 00000000
Accession #: 000-00-0118

HED Records Reference Center
5/16/2007